

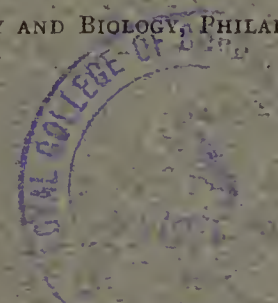
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RETURN TO NORMAL DIET, ON THE GROWTH OF
THE BODY AND CENTRAL NERVOUS SYSTEM OF
ALBINO RATS.

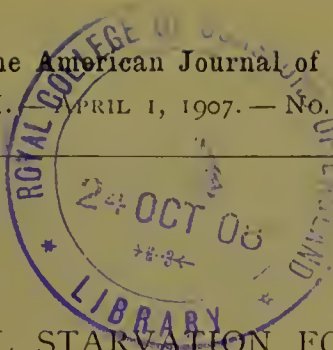
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EFFECT OF PARTIAL STARVATION FOLLOWED BY A RETURN TO NORMAL DIET, ON THE GROWTH OF THE BODY AND CENTRAL NERVOUS SYSTEM OF ALBINO RATS.

By SHINKISHI HATAI.

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IN my previous research (:04) on the effect of partial starvation on the brain of the albino rat, it was shown that in the experimented rats, fed with starch, beef fat, and water for twenty-one days (younger group, rats thirty to forty days old; older group, rats one hundred and fifty to two hundred days old), not only the growth of the brain was stopped, but brain substance was lost, the actual loss from the weight before starvation being, on the average, 4.67 per cent. In such experimented animals, also, the percentage of water in the brain was diminished (79.08 per cent control, and 78.84 per cent experimented) and of the ether-alcohol extracts increased (46.69 per cent control, and 47.61 per cent experimented — Hatai, :04).

As the absolute weight of the brain in the starved group was diminished, and as the relative amount of the extracts was increased, the writer inferred that the protein substances had been most affected. The total loss in the body weight in the experimented rats at the end of twenty-one days was 29.7 per cent.

Having established the fact that the brain is definitely modified as the result of partial starvation for twenty-one days, the next question was:

Can the nervous system thus affected recover when the animal is returned to a normal diet? The present research was undertaken in order to answer this question.

Altogether thirty-two rats, representing seven litters, were used. One half of each litter was subjected to partial starvation, and the other half used for control. The rats were so grouped that at the beginning of the observation the average body weight in the control group balanced that in the experimented. As soon as the young

albino rats reached thirty days of age, the experimented groups were fed with starch (Oswego cornstarch) and water alone,¹ while the control groups were fed with the usual diet, — corn, cabbage, milk, bread, meat, etc. The supply of food for both groups was abundant. After twenty-one days of starvation the experimented rats were at once put on the full normal diet, and then fed for the succeeding one hundred and forty-nine days with the same diet as was given to the control group. When the rats became two hundred² days old, they were killed, and the weight of the central nervous system, percentage of water, and percentage of the ether-alcohol extracts were determined. The dissection of the rats, and the procedure for the determination of weight, etc., were carried out with all the precautions used in the previous experiments.

Body weight. — As is shown in Table I, the initial weight of the experimented male rats was slightly greater (6.5 per cent) than that of the male controls, while that of the experimented females was slightly less (5.5 per cent) than that of the female controls. As the result of the partial starvation, the loss in the body weight of the experimented group was 24 per cent in the male, and 21 per cent in the female, while the increase in the control group for the same period amounted to 44.2 per cent in the male, and 46.4 per cent in the female. Thus, after twenty-one days (*i. g.*, at the age of $30 + 21 = 51$ days), the difference in the weight between the control and experimented groups became very large, amounting to 55 per cent in the male, and 60 per cent in the female, the weight of the control group being taken as the standard.

In my previous research the loss in the weight (younger series, thirty to forty days old) after twenty-one days of starvation was even greater; the average for both sexes being 32 per cent, as contrasted with 23 per cent in the present research. It must be remembered, however, that in the earlier experiments the rats were slightly older. Thus the greater loss in weight in the previous case was, perhaps, in some measure due to the reduction of fat.

After twenty-one days of starvation the experimented rats showed marked changes, the vertebral spines were evident, the trunk slightly curved, the pink color had entirely disappeared from the soles of the feet as well as from the external ear, the eyelids were partly closed,

¹ The beef fat was omitted in the present experiment.

² It was found in our laboratory that the albino rats of two hundred days old are fully matured. The sexual maturity takes place at about seventy days of age.

and movements were rather unsteady. The rats in this state were removed to the other cages and at once given a full normal diet. The rapidity of recuperation was surprising, as it took only three or four days for them to return to their initial weight.

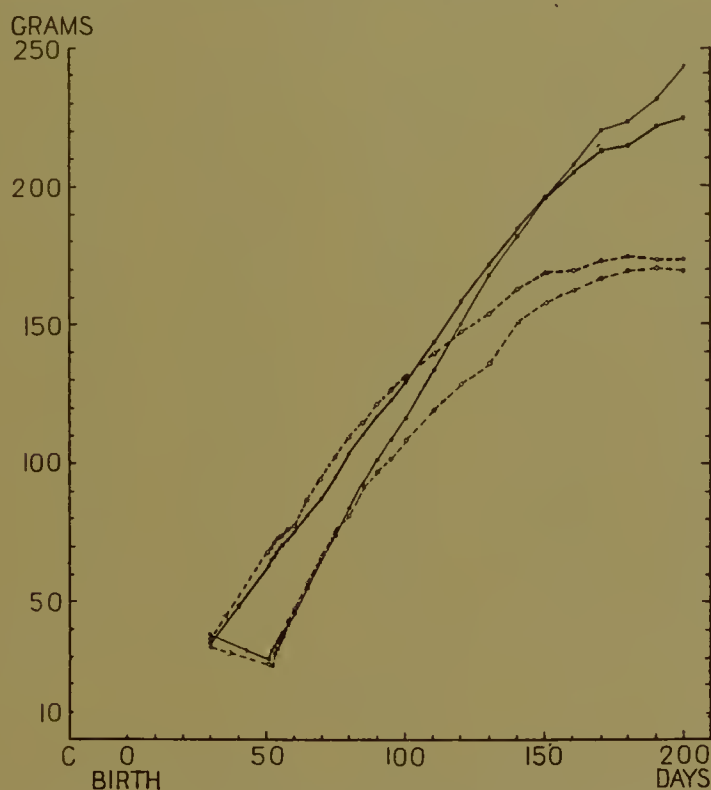


FIGURE 1. — Curves showing the body weights of albino rats at different ages. *C*, conception, and *O*, the date of birth twenty-one days after conception. •—• Males Starved. ○.....○ Female Starved. —•—• Male Control. ○.....○ Female Control.

It was naturally asked whether or not the mere distention of the stomach was responsible for the rapid recovery in the body weight. A careful examination, however, showed that this was not the case. Within three to four days almost all the evidences of disturbed nutrition, enumerated above, entirely disappeared. The pink color reappeared in the soles of the feet and the external ear; the eyes were held widely opened, the trunk became straight. The movements, however, were not so steady or so active as in the normal rats. An interpretation of this rapid recovery is postponed until the composition of the urine during such a period, as well as some other points, have been determined.

The daily increase or decrease in weight is shown in Fig. I. At

TABLE I.

| CONTROL RATS (MALES). | | | | | | |
|-------------------------|-------------------|--------|-----------|-----------|--------------------|-----------|
| Body weight. | | | Weight of | | Percentage, water. | |
| Initial. | After 21 days. | Final. | Brain. | Sp. cord. | Brain. | Sp. cord. |
| | | | | | per cent. | per cent. |
| 23.6 | 60.3 | 211.5 | 1.7810 | 0.5520 | 77.36 | 69.61 |
| 25.6 | 48.6 | 233.8 | 1.8030 | 0.5348 | 77.79 | 70.26 |
| 27.2 | 56.0 | 205.0 | 1.7988 | 0.5614 | 77.79 | 69.50 |
| 28.2 | 54.0 | 188.4 | 1.7214 | 0.5330 | 77.13 | 69.60 |
| 31.4 | 55.6 | 228.8 | 1.9264 | 0.5894 | 77.28 | 69.90 |
| 36.2 | 59.8 | 199.2 | 1.7641 | 0.5168 | 77.60 | 70.54 |
| 42.7 | 76.4 | 223.4 | 1.8847 | 0.5814 | 77.27 | 69.38 |
| 43.2 | 74.2 | 211.2 | 1.8634 | 0.5415 | 77.80 | 69.56 |
| 58.6 | 83.0 | 318.4 | 2.1862 | 0.6548 | 77.51 | 69.06 |
| | | | | | | |
| AVERAGES. | | | | | | |
| 35.2 | 63.1 | 224.4 | 1.8587 | 0.5628 | 77.50 | 69.71 |
| CONTROL RATS (FEMALES). | | | | | | |
| 24.2 | 72.4 | 161.2 | 1.6644 | 0.4770 | 77.60 | 70.10 |
| 26.5 | 59.0 | 141.3 | 1.6864 | 0.4866 | 77.44 | 69.21 |
| 26.8 | 54.8 | 154.2 | 1.7018 | 0.4864 | 77.65 | 69.10 |
| 42.5 | 75.8 | 188.8 | 1.8664 | 0.5582 | 77.34 | 69.13 |
| 46.2 | 74.6 | 201.6 | 1.9063 | 0.5834 | 77.39 | 69.22 |
| 51.6 | 70.2 | 188.2 | 1.9272 | 0.5587 | 77.58 | 69.62 |
| | | | | | | |
| AVERAGES. | | | | | | |
| 36.3 | 67.8 | 172.6 | 1.7905 | 0.5250 | 77.50 | 69.40 |

TABLE I (Continued).

| EXPERIMENTED RATS (MALES). | | | | | | |
|------------------------------|-----------|-----------|--------|--------------|----------------|----------|
| Percentage, water. | | Weight of | | Body weight. | | |
| Sp. cord. | Brain. | Sp. cord. | Brain. | Final. | After 21 days. | Initial. |
| per cent. | per cent. | | | | | |
| 71.06 | 78.05 | 0.5108 | 1.7930 | 199.7 | 20.8 | 27.2 |
| 69.97 | 77.84 | 0.5482 | 1.7507 | 196.3 | 22.8 | 27.5 |
| 70.95 | 77.90 | 0.4978 | 1.6138 | 194.0 | 22.2 | 28.8 |
| 69.79 | 77.74 | 0.5714 | 1.9514 | 228.7 | 23.8 | 31.1 |
| 70.20 | 77.82 | 0.5940 | 2.0681 | 262.0 | 25.0 | 32.0 |
| 70.47 | 77.68 | 0.5460 | 1.7696 | 215.8 | 26.4 | 32.0 |
| 69.97 | 77.91 | 0.5902 | 1.8779 | 256.0 | 30.4 | 40.8 |
| 69.66 | 77.39 | 0.5988 | 1.9493 | 281.0 | 32.2 | 43.9 |
| 69.05 | 77.52 | 0.5926 | 1.9774 | 259.0 | 38.2 | 52.2 |
| 69.46 | 77.61 | 0.7162 | 2.1154 | 327 0 | 42.4 | 60.6 |
| AVERAGES. | | | | | | |
| 70.05 | 77.75 | 0.5766 | 1.8866 | 242.0 | 28.4 | 37.6 |
| EXPERIMENTED RATS (FEMALES). | | | | | | |
| 71.11 | 77.90 | 0.4120 | 1.5614 | 130.0 | 20.2 | 24.0 |
| 70.81 | 78.01 | 0.4520 | 1.5696 | 138.2 | 21.4 | 24.6 |
| 69.56 | 77.64 | 0.5152 | 1.6800 | 176.0 | 28.9 | 36.1 |
| 69.46 | 77.91 | 0.5804 | 1.8472 | 198.8 | 29.7 | 36.9 |
| 70.85 | 77.82 | 0.4858 | 1.6372 | 152.0 | 26.3 | 37.8 |
| 69.92 | 77.60 | 0.5593 | 1.8811 | 181.0 | 32.4 | 40.0 |
| 69.21 | 77.41 | 0.5574 | 1.8608 | 199.0 | 30.0 | 40.9 |
| AVERAGES. | | | | | | |
| 70.10 | 77.75 | 0.5089 | 1.7196 | 167.8 | 27.0 | 34.3 |

the end of two hundred days the final weight in the experimented and in the control was 242 and 224 gm. respectively, in the case of the males, and 173 gm. and 168 gm. in the case of the females; that is, the experimented male rats were slightly heavier (7.4 per cent) than in the controls, while in the case of the females the control rats were the heavier (2.5 per cent).

The comparison between the initial and final weight is shown in Table II.

TABLE II.

| | Body weight. | | | Total gain. | Ratio between initial and final. |
|------------------------|--------------|----------------|--------------------|-------------|----------------------------------|
| | Initial. | After 21 days. | Final. | | |
| Male, controls . . . | 35.2 | 63.1 | 224.4 | 189.2 | 1 : 6.37 |
| Male, experimented . . | 37.6 | 28.4 | 242.0 | 204.4 | : 6.43 |
| Female, controls . . . | 36.3 | 67.8 | 172.6 ¹ | 136.3 | : 4.75 |
| Female, experimented . | 34.3 | 27.0 | 167.8 ¹ | 133.5 | : 4.89 |

From the above it is seen that the absolute gain in weight is slightly greater in the experimented males, and slightly smaller in the experimented females, as compared with their controls. The ratios, however, show that the relative gain is approximately the same in both experimented and control groups, although slightly greater in the case of the experimented rats in both sexes.

I therefore conclude that so far as the body weight is concerned, the experimented rats have completely recovered from the effect of the twenty-one days of partial starvation.

It has been frequently observed by different investigators — Coudeureau ('69), Pagliani ('79), and others — that the growth of the body in recuperation is very rapid in the children whose growth has been temporarily disturbed by illness or other unfavorable conditions. This observation is well supported by the present experiments. As is shown in Table I, as well as in Fig. I, the recovery in the weight is most astonishing, especially during the first three or four days, within which time the starved rats regain the weight lost during the twenty-one days of starvation. Later the increase in weight is very steady, though not as rapid as during the first few days, until the rat has reached the age of one hundred and fifty days, and after this age increase in weight is relatively slow.

What will happen to such rats during the later portions of the

¹ The body weight in both control and experimented is small for the age.

span of life has yet to be determined in order to answer the question whether this partial starvation in early life has any influence either on longevity or the onset of old age.

Weight of brain and spinal cord.—After the body weight had been taken, the brain and spinal cord were removed separately, and their weights were carefully determined. The spinal cord was

TABLE III.

| | Body weight. | Encephalon. | Sp. cord. |
|--------------------------|--------------|-------------|-----------|
| Male, controls | 224 | 1.8587 | 0.5682 |
| Male, experimented . . | 242 | 1.8866 | 0.5766 |
| Female, controls | 173 | 1.7905 | 0.5250 |
| Female, experimented . . | 168 | 1.7196 | 0.5089 |

severed from the encephalon at the tip of the calamus scriptorius. The spinal roots were cut off as close to the cord as possible. The results obtained are seen in Table III.

As it stands, the weight of the central nervous system in the experimented male is heavier, and in the experimented female lighter, when compared with the corresponding controls. Since the brain weight is closely correlated with the body weight, we should expect a heavier brain weight in the heavier individuals, and therefore it is desirable to determine whether or not the brain weights found in the experimented rats correspond with the given body weights. Dubois ('98) found that in man, at maturity, the brain weights were related as the fourth roots of the body weights.

Dhéré and Lapique ('98) have determined a like relation for dogs of different sizes where they found a good accordance between the observed and calculated results. An application to the present data of this law given by Dubois for the human brain weights, shows that in the case of the males 1.8866 gm. of brain in the experimented males should correspond to the body weight of 238.3 gm., instead of 242 gm., when the relations in the control group are used as a standard. The difference (3.7 gm.) is too small to be considered significant. It is therefore quite safe to conclude that so far as the relation between brain weight and body weight in the male is concerned, the starvation effect has been completely removed. In the case of the female we have some difficulty in applying Dubois' law, since the brain weight in the control group is too high¹ for the given body weight. Accord-

¹ This fact was determined by examining some ten records preserved in our archives, for female rats having a body weight of about 173 gm.

ing to Dubois' law, the figures for the control group being taken as the standard, a brain of 1.7196 gm. found in the experimented group should correspond to body weight of 147.3 gm., instead of 168 gm., as observed. It was found that according to our standard curve 1.7196 gm. of brain weight there corresponds to the body weight of 162 gm., or 6 gm., less than that observed. This difference is negligible in view of the variability in this relation, and therefore it seems

TABLE IV.

| | Percentage of water. | |
|--------------------------------|--------------------------|------------------------|
| | Encephalon. per cent. | Sp. cord. per cent. |
| Male, controls | 77.50 | 69.71 |
| Male, experimented | 77.75 | 70.05 |
| Female, controls | 77.50 | 69.40 |
| Female, experimented | 77.75 | 70.10 |

safe to conclude that in the experimented female group partial starvation has not permanently modified the relation of brain weight to body weight.

In regard to the weight of the spinal cord, it is clearly shown that the cord also follows body weight in the same manner as does the brain, but the details have not been worked out.¹

Percentage of water in the central nervous system. — From Table IV it is clearly seen that percentage of water in both encephalon and spinal cord is higher in the experimented rats than in the control rats.

On the average, the difference between the experimented and control is 0.25 per cent in the encephalon of both sexes, and 0.34 per cent in the male spinal cord, and 0.70 per cent in the female, always in favor of the experimented groups. Although the difference shown is small, nevertheless it is significant, since the difference appears in all but one instance when the representatives of the same litter are compared.

From unpublished observations in this laboratory, it has been concluded that during normal growth the percentage of water in the

¹ An application of Dubois' law to the weight of the spinal cord shows that, when the relations in the control group are used as a standard, 0.5766 gm. of spinal cord in the experimented males correspond to the body weight of 247.4 gm. (difference 5.4 gm.), and 0.5089 gm. of the experimented female spinal cord to 152.8 gm. of the body weight (difference, 15.2 gm.). These calculated values of the body weight agree with those calculated from the brain weight, indicating that the relation of the spinal cord to the body is similar to that of the brain.

TABLE V.

| LITTER 1. | | | | | |
|---|--------------------|--------------------|--------------------|--------------------|--------------|
| CONTROL RATS. | | | EXPERIMENTED RATS. | | |
| Body weight. | Percentage, water. | | Percentage, water. | | Body weight. |
| | Brain. | Sp. cord. | Sp. cord. | Brain. | |
| 223.4 M. | per cent. 77.27 | per cent. 69.38 | per cent. 69.66 | per cent. 77.39 | M. 281.0 |
| 188.8 F. | 77.34 | 69.13 | 69.35 | 77.41 | F. 199.0 |
| LITTER 2. | | | | | |
| 318.4 M. | 77.51 | 69.06 | 69.46 | 77.61 | M. 327.2 |
| 201.6 F. | 77.39 | 69.22 | 69.46 | 77.91 | F. 198.8 |
| 188.2 F. | 77.58 | 69.22 | 69.90 | 77.60 | F. 181.0 |
| | | | 69.56 | 77.64 | F. 176.0 |
| LITTER 3. | | | | | |
| 211.2 M. ¹ | 77.80 | 69.56 | 69.05 | 77.52 | M. 259.0 |
| LITTER 4. | | | | | |
| 199.2 M. | 77.60 | 70.54 | 69.97 | 77.91 | M. 256.2 |
| | | | 70.47 | 77.68 | M. 215.8 |
| | | | 70.85 | 77.82 | F. 152.0 |
| LITTER 5. | | | | | |
| 233.8 M. | 77.79 | 70.26 | 70.20 | 77.82 | M. 262.0 |
| 228.8 M. | 77.28 | 69.90 | 71.06 | 78.05 | M. 199.7 |
| 205.0 M. | 77.79 | 69.50 | 70.95 | 77.90 | M. 194.0 |
| 188.4 M. | 77.13 | 69.60 | 71.11 | 77.90 | F. 130.0 |
| 154.2 F. | 77.65 | 70.10 | | | |
| ¹ Litter 3 alone is an exceptional case where the percentage of water in the control is higher than in the experimented rat. | | | | | |

TABLE V (*continued*).

| LITTER 6. | | | | | |
|---------------|-------------------|-----------|--------------------|-----------|--------------|
| CONTROL RATS. | | | EXPERIMENTED RATS. | | |
| Body weight. | Percentage, water | | Percentage, water. | | Body weight. |
| | Brain. | Sp. cord. | Sp. cord. | Brain. | |
| | per cent. | per cent. | per cent. | per cent. | |
| 211.5 M. | 77.36 | 69.61 | 69.79 | 77.74 | M. 228.7 |
| 141.3 F. | 77.44 | 69.21 | 69.97 | 77.84 | M. 196.3 |
| LITTER 7. | | | | | |
| 161.2 F. | 77.60 | 69.10 | 70.81 | 78.01 | F. 138.2 |

nervous system of the rat is mainly a function of its age, and is but slightly modified by the weight of the central nervous system or of the size of the body (Donaldson). In these experiments, however, the relation of age to the nervous system is considerably modified in the experimented rats, since not only the growth of the nervous system has been completely stopped for twenty-one days, but the percentage of water was diminished (79.08 per cent control, and 78.84 per cent experimented — Hatai,:04) by this treatment. Therefore the higher percentage of water found in the central nervous system of the experimented rats after recovery may mean one of two things: (1) As the result of partial starvation, the destructive process which has been traced (see previous paper, Hatai,:04,) might produce a diminution of nerve tissue, and the relatively higher content of water might be due merely to an accumulation of fluid occupying the spaces which had been so developed; (2) It may indicate a much more active metabolic process, and be an indication of recuperative activity.

The second assumption seems the more probable, since the weight of the central nervous system was normal in relation to the body weight, indicating that there was not a mere accumulation of the fluid occupying newly formed spaces, for this would have tended to reduce the brain weight.

Recently Watson (:05) made observations on the effect of the bearing of young upon the body weight and the weight of the central nervous system of female albino rats, where he has shown that the brain and spinal cord of the mated individuals contained a slightly higher percentage of water.

He gives the following percentage values:

| | Percentage of water. | |
|---------------------------------|----------------------|------------------------|
| | Brain. per cent. | Sp. cord. per cent. |
| Mated (average — 8 rats) . . . | 77.47 | 68.51 |
| Unmated (average — 10 rats) . . | 77.37 | 68.29 |

Watson's experiments may be considered analogous to mine, as he is also dealing with animals that have passed through a period of partial starvation, since during lactation the mother loses body weight to quite an extent (Minot, '91; Watson, :05). Although it is impossible at the present moment to make any definite statement, our observations on partial starvation suggest that the higher percentage of water found in the rats bearing young might have been produced as the effect of temporary retardation of the growth of the nervous

TABLE VI.

| | Percentage of extracts. | |
|------------------------------|--------------------------|------------------------|
| | Encephalon. per cent. | Sp. cord. per cent. |
| Male, controls | 50.61 | 68.83 |
| Male, experimented | 50.36 | 68.54 |
| Female, controls | 49.56 | 68.87 |
| Female, experimented | 49.16 | 68.40 |

system followed by recovery. This can be determined only by a study of the nervous system during the period of greatest retardation in rats bearing young.

It remains, moreover, to be determined whether or not our experimented rats will in this respect recover entirely from this condition which is produced by the twenty-one days of partial starvation.

In the normally grown rats the percentage of extracts in the nervous system is also a function of age, and is inversely related to the percentage of water (Donaldson). Thus the determination of the percentage of extracts would furnish us further evidence as to the normal condition of the growth of the nervous system with respect to age and to the percentage of water.

It is clear from the preceding Table VI that the percentage of ex-

tracts is less in the experimented group in both encephalon and spinal cord than in the control. In the case of the encephalon 0.25 per cent in the male and 0.40 per cent in the female, and in the case of the spinal cord, 0.29 per cent in the male and 0.47 per cent in the female are in favor of the control rats. These are the results that one would expect. It is therefore concluded that the amount of extract, as compared with the residue, found in the nervous system of the experimented rats is normal with respect to the age and percentage of water in that organ.

CONCLUSIONS.

From what has been presented, the following conclusions are drawn:

(1) So far as the weight of the body and central nervous system are concerned, the effect of a twenty-one day period of partial starvation on albino rats thirty days old is eventually completely compensated.

(2) The chemical composition of the brain and spinal cord is, however, not entirely free from the effect, as is indicated by the higher percentage of water, and lower percentage of ether-alcohol extracts, in the experimented rats, as compared with the controls.

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